

FIG. 2A

LYMPHOCYTES

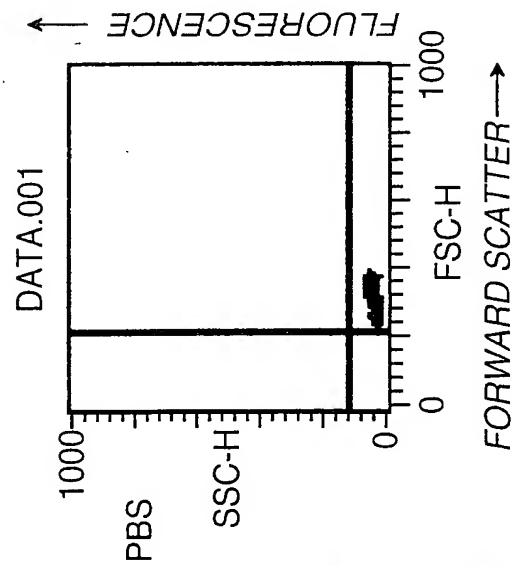


FIG. 2B

GRANULOCYTES

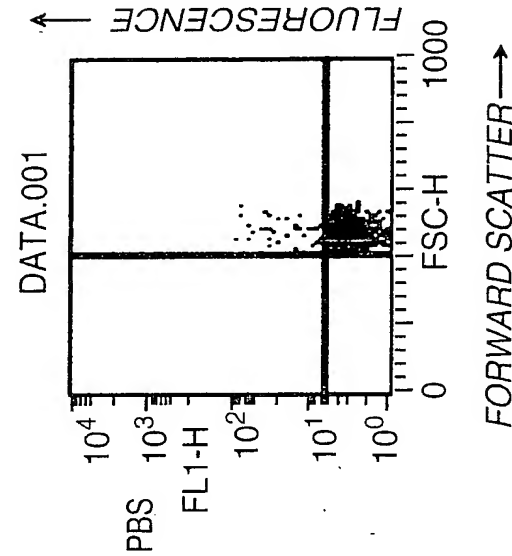


FIG. 2C

MONOCYTES

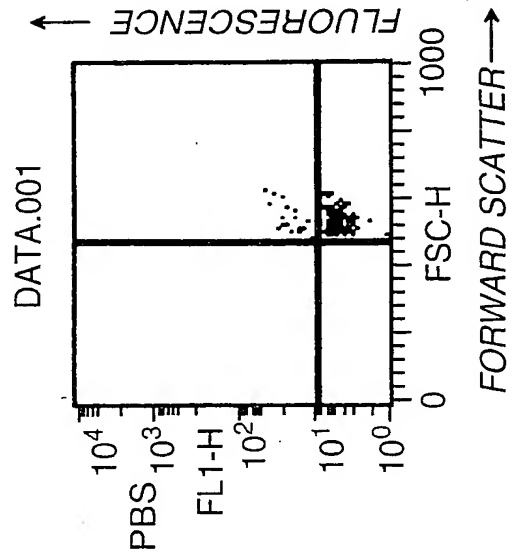


FIG. 2D

LYMPHOCYTES

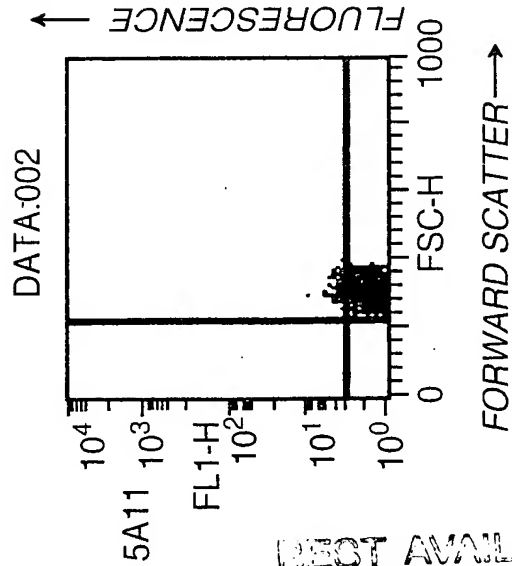


FIG. 2E

GRANULOCYTES

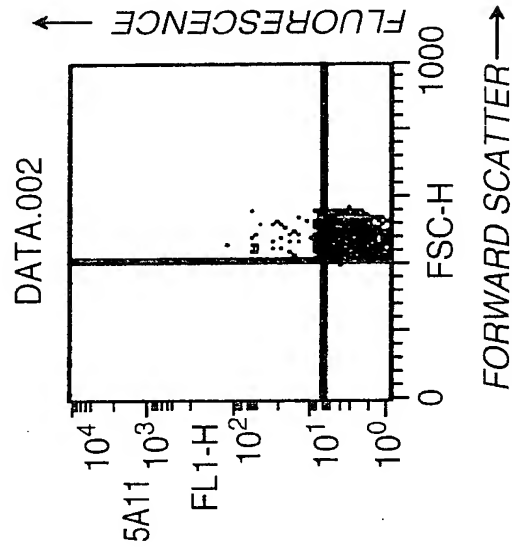


FIG. 2F

MONOCYTES

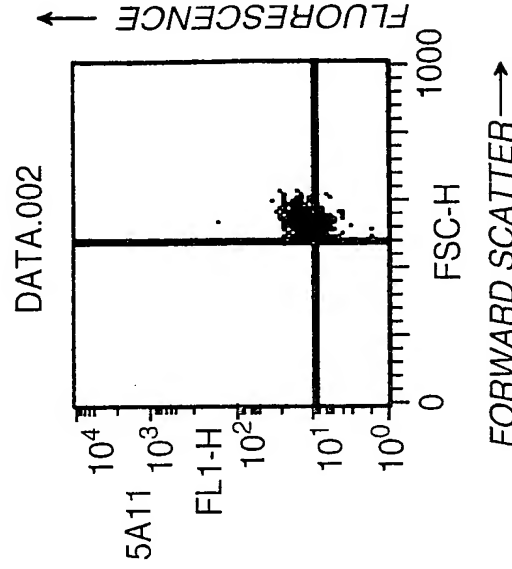


FIG. 2G

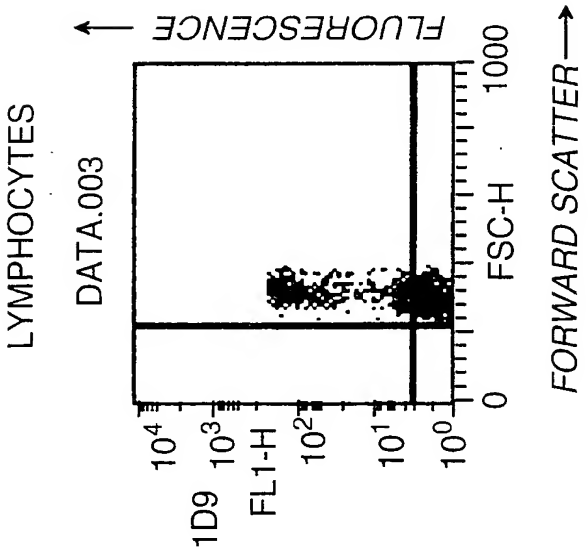


FIG. 2H

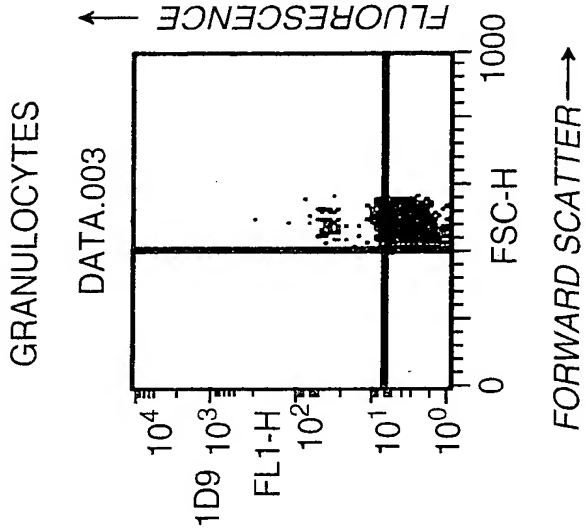


FIG. 2I

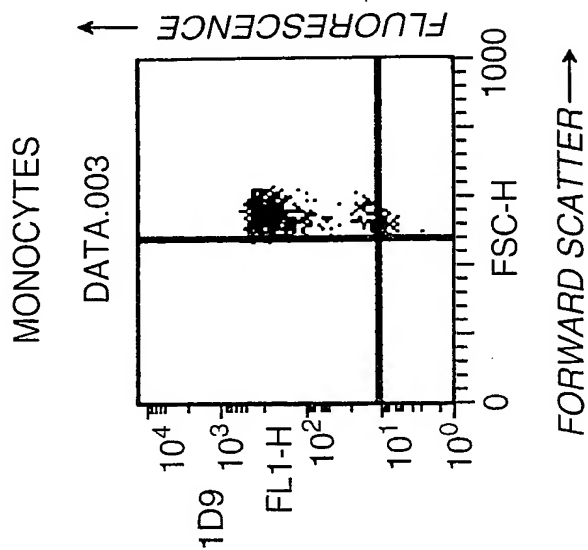


FIG. 2J

LYMPHOCYTES

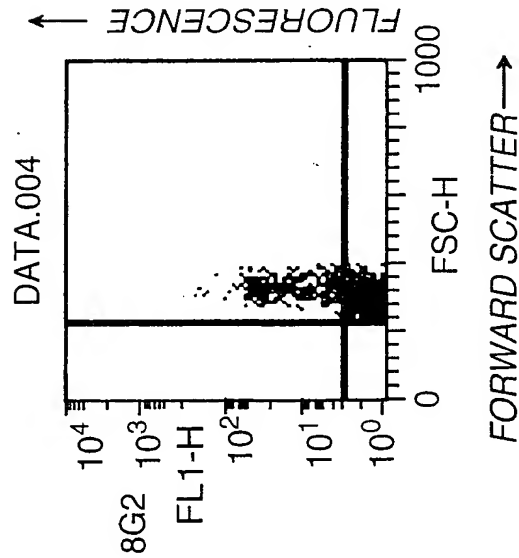


FIG. 2K

GRANULOCYTES

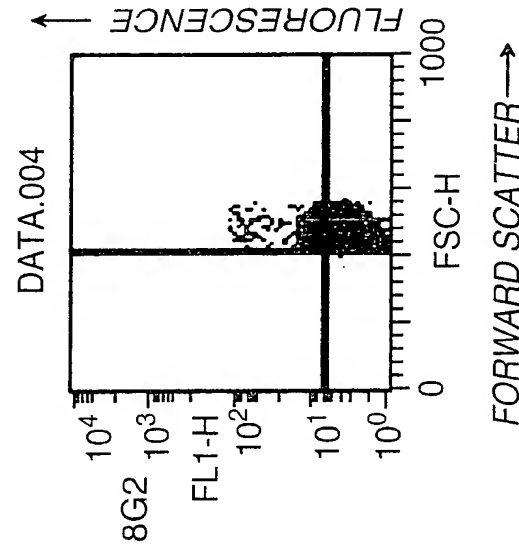


FIG. 2L

MONOCYTES

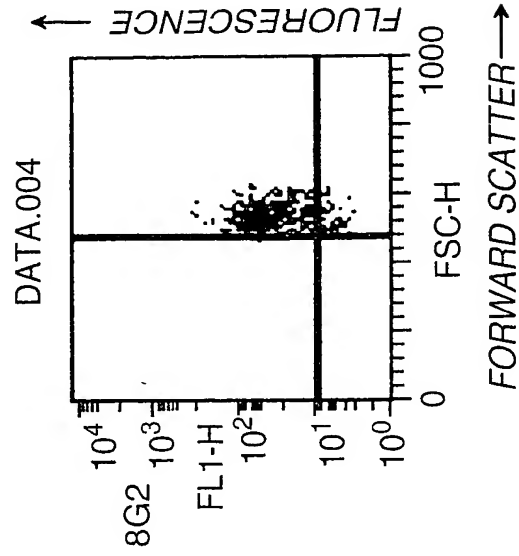


FIG. 3A

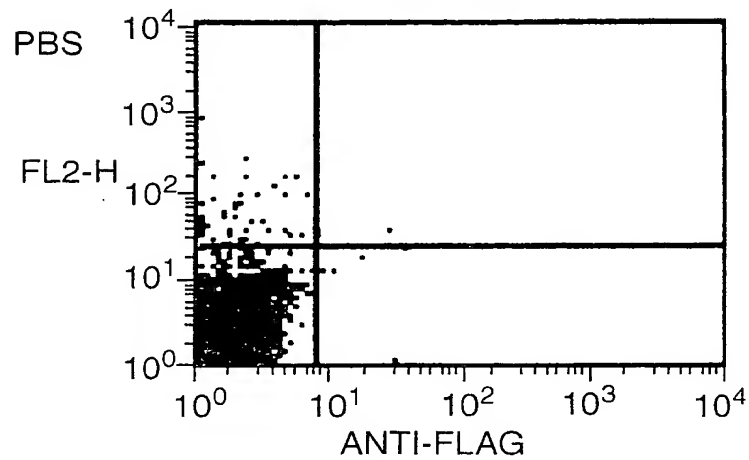


FIG. 3B

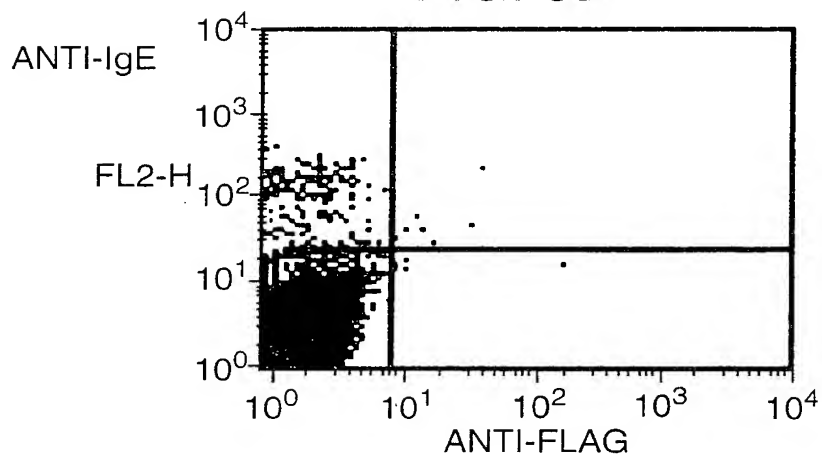


FIG. 3C

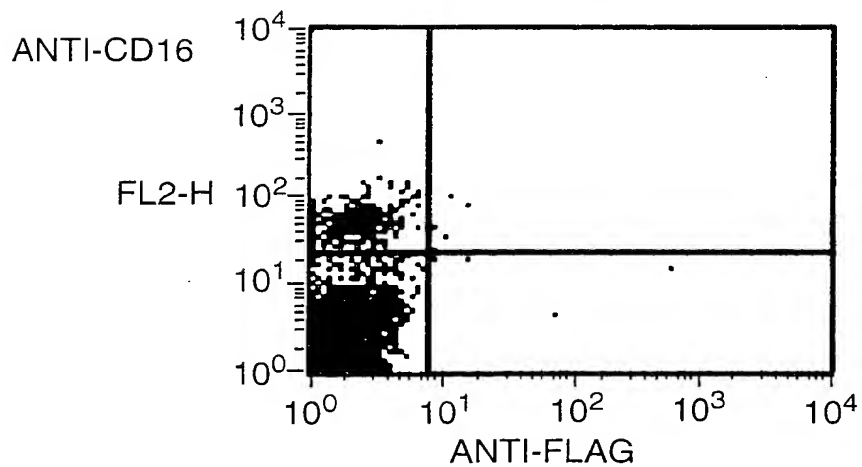


FIG. 3D

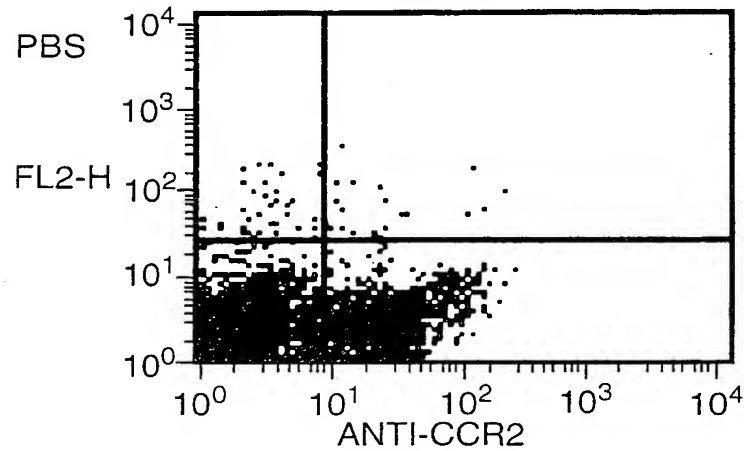


FIG. 3E

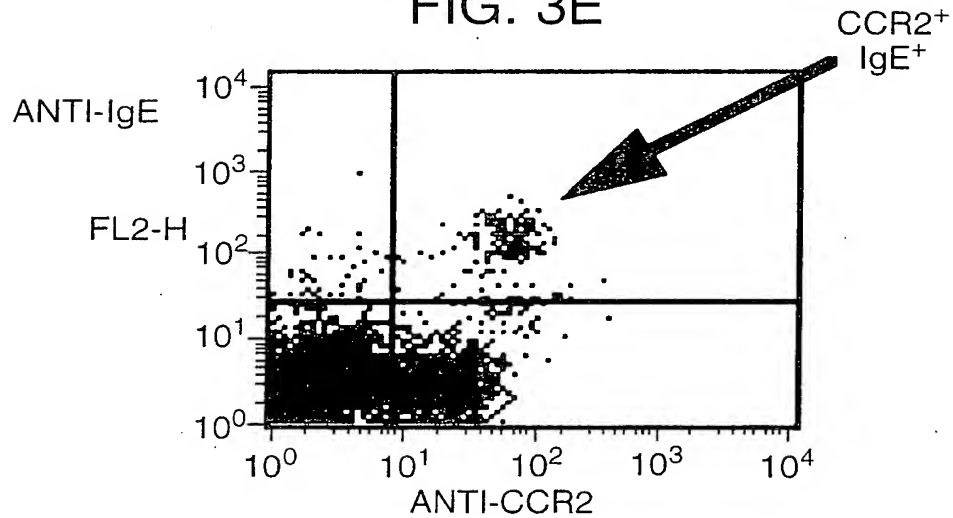


FIG. 3F

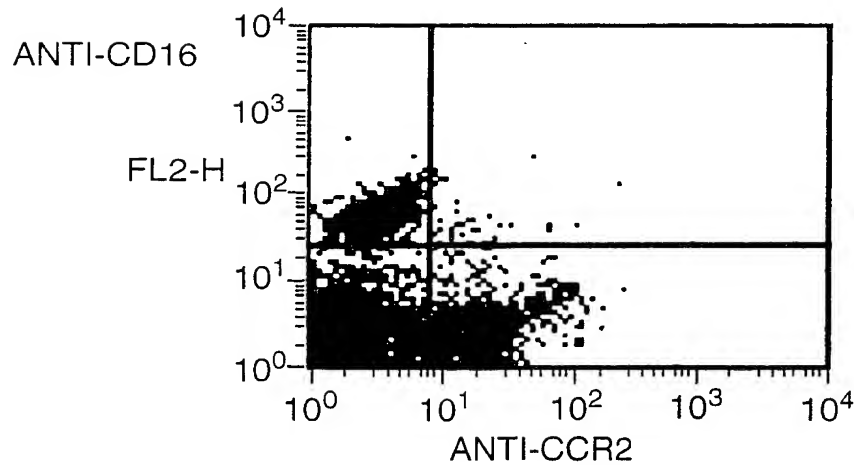


FIG. 3G

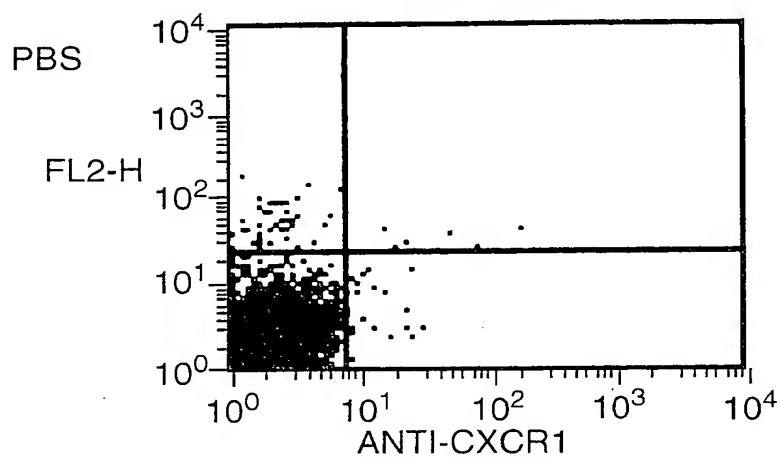


FIG. 3H

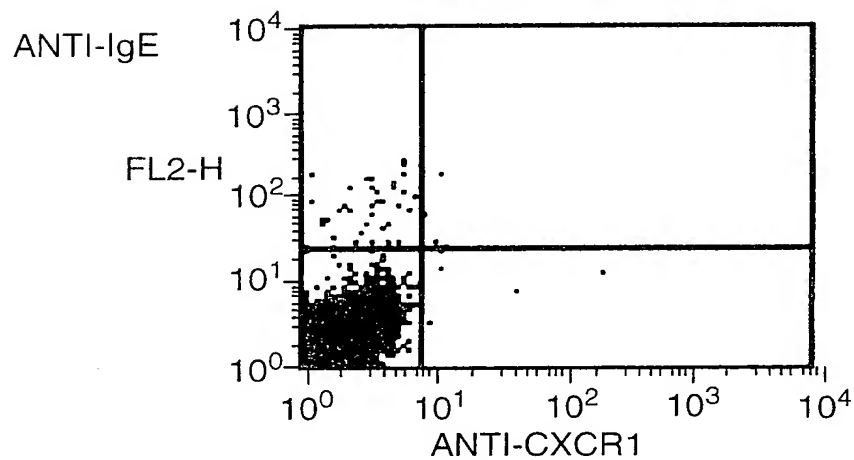
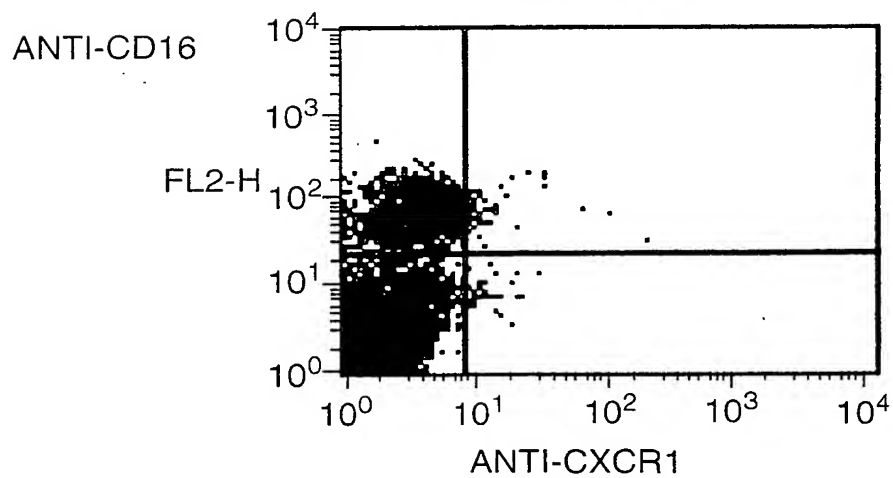


FIG. 3I



■

1C6 (anti CXCR3)

●

ID9 (anti CCR2b)

ID9 (µg/mL)		
	Value	Error
IC50	0.0037891	0.00062521
Hill	1.0185	0.15131
Bmax	105.63	2.6422
Bmin	11.518	1.9284
Chisq	280.01	NA
R	0.9948	NA

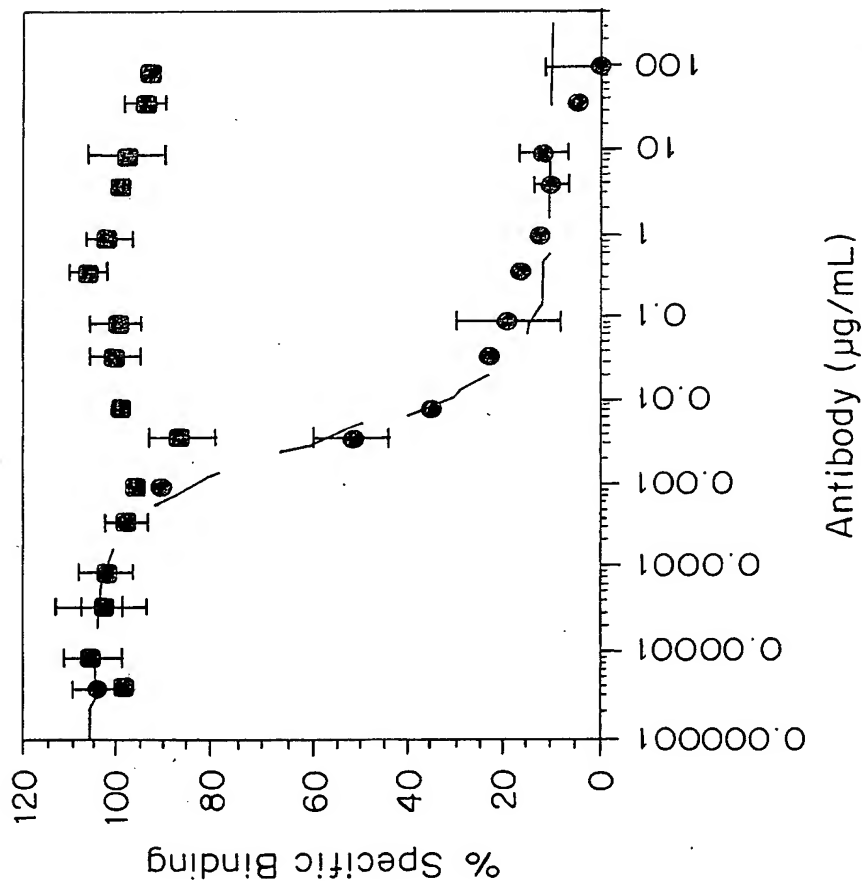


FIG. 4

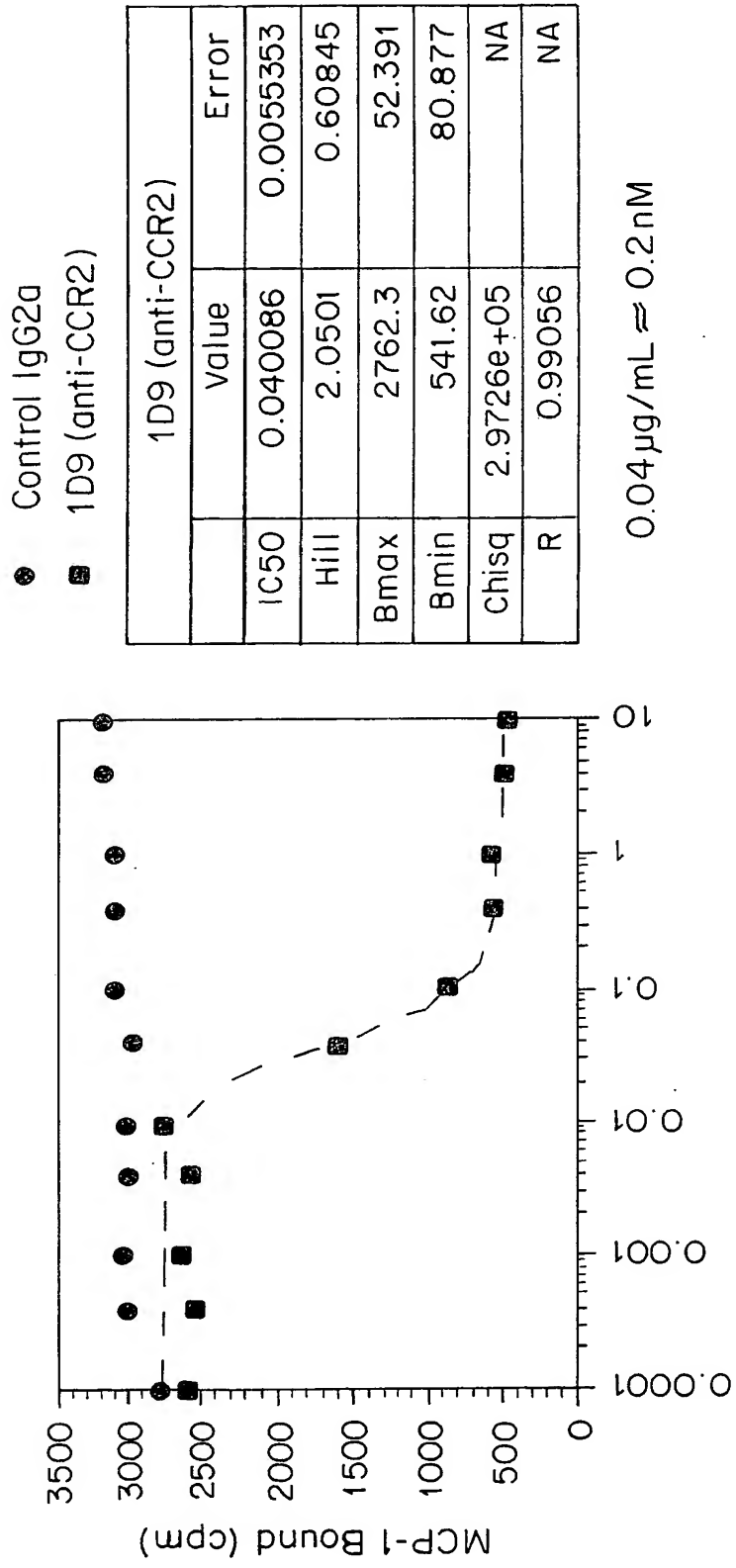


FIG. 5

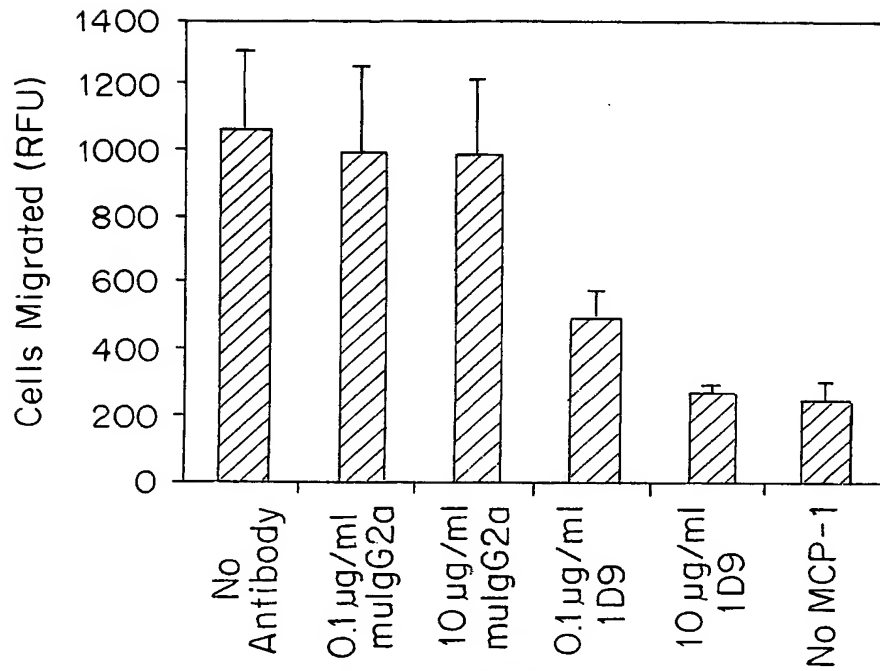


FIG. 6A

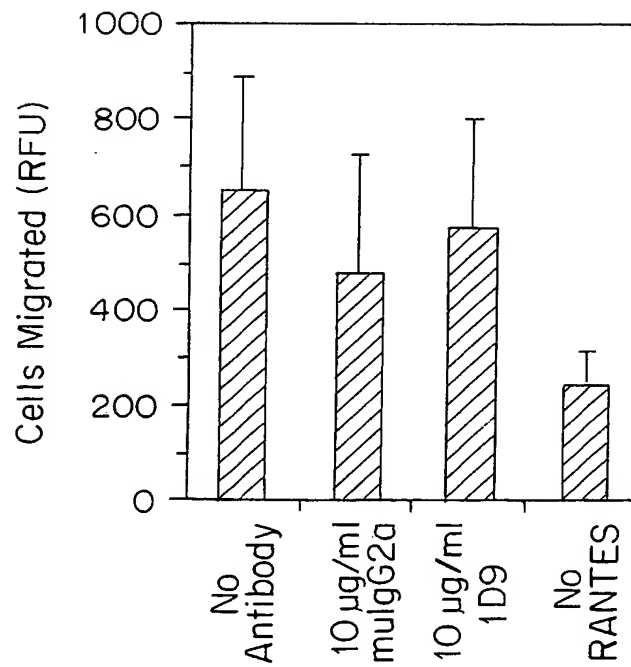


FIG. 6B

1 DVVMTQTPLT LSVTVGHPAS ISCKSSQSLL DSDGKTFLNW LLQRPGQSPK

51 RLIYLVSKLD SGVPDRFTGS GSGTDFTLKI SRVEAEDLGV YYCWQGTHTFP

101 YTFGGGGTKLE IK

Figure 7

1 EVQLVESGGG LVQPKGSLKL SCAASGFSEF **AYAMNWVRQA** PGKGLEWVAR

51 **IRTKNNNYAT YYADSVKDRY** TISRDDSESM LFLQMNNLKT EDTAMYYCVT

101 **FYGNGVWGTG** TTVTVSS

Figure 8

Chothia Canonical Classes

- L1 (16 amino acids) = Class 4
Key residues: **2(V)**, 25(SA), 29(L), 33(L), **71(F)**
- L2 (7 amino acids) = Class 1
Key residues: **48(IV)**, 51(AT), 52(ST), **64(G)**
- L3 (9 amino acids) = Class 1
Key residues: 90(QNH), 95(P)

Martin Canonical Classes

- L1 (16 amino acids) = Class 4/16A
Key residues: **2(V)**, **4(ML)**, **23(C)**, 25(SSP), 26(SN),
27(Q), 29(LI), 30A(HL), 30B(S),
30C(NDS), 30D(G), 32(YS), 33(LF),
34(HEN), **35(W)**, 51(V), **71(F)**, **88(C)**,
90(Q), 92(TS), 93(H)
- L2 (7 amino acids) = Class 1/7A
Key residues: **23(C)**
- L3 (9 amino acids) = Class 1/9A
Key residues: **2(IVL)**, **3(VQLE)**, **4(ML)**,
28(SNDTE), 30(DYLVISNFGHT),
31(SNTKG), 32(FYNAHSR),
33(MLVIF), **88(C)**, 89(QSGFL),
90(QNH), 91(NFGSRDHTYV),
92(NYWTSRQHAD),
93(ENGHTSRAQHAD),
94(DYTVLHNNIWPS), 95(P),
96(PLYRIWF), 97(T), **98(F)**

Figure 9

Chothia Canonical Classes

- H1 (5 amino acids) = Class 1
Key residues: 24(AVG), 26(G), 27(FY)
- H2 (19 amino acids) = Class 4
Key residues: 54(S), 55(Y), 71(R)

Martin Canonical Classes

- H1 (5 amino acids) = Class 1/10A
Key residues: 2(VIG), 4(LG), 20(LIMV), 22(C),
24(TAGVS), 26(G), 29(IFLS),
32(IHYFTNCED), 33(AWGTLV),
34(IVMW), 35(HENQSYT), 36(W),
48(IMLV), 51(LIVTSN),
69(ILFMV), 78(ALVYF), 80(LM),
90(YF), 92(C), 94(RKGSNH),
102(YHVISDG).
- H2 (19 amino acids) = Class 7/12B
Key residues: 47(W), 50(RQ), 51(I), 59(Y), 69(I),
71(R), 78(LV)

Figure 10

-----L3-----

1D9RK_D V_K CDR grafted 1D9 V_K region, with back mutations at F36L, Q37L, Q100G and Q17H, and the additional 107K insertion.

Figure 11

CDRs											
-----H1=====H2=====H3-----											
Kabat Numbers	1	2	3	4	5	6	7	8	9	1	1
1234567890											

Figure 12

Amino Acid Sequence

Sequence Identical
Name Residues

1D9 V _K	114	DVYMTQTPLTSLVTGHPASISCKSSQSLIDS-DGKTFLNLLQRPQSPKRLIYLVSKLD SGVPDRFTGSGSGTDFTLKISRVEAEDLGYYVCWQGTFFP
70/3	97I.Q.....Y.....Y.....V.....V.....
70/1	94I.Q.....Y.N.Y.....Y.....V.....X.M.D.....
70/2	82XLHS.....I.Q.....Y.N.Y.....V.P.....S.....XP.....
V-IB	76S.P.SL.DQ.....R.....VH.N.N.Y.Y.Y.K.....L.R.NRF.....S.....F.F.....V.
V-1C	75S.P.SL.DQ.....R.....IVH.N.N.Y.E.Y.K.....L.K.NRL.....S.....F.S.V.
V-1A/K5.1/K5.1	75S.P.SL.DQ.....R.....VH.N.N.Y.H.Y.K.....L.K.NRF.....S.....F.S.S.V.
V-1C/V1A5/K1A5	74	..L.....S.P.SL.DQ.....R.....IVH.N.N.Y.E.Y.K.....L.K.NRF.....S.....F.S.V.
K18.1	73	.A.....S.P.SL.DQ.....R.....EN.N.N.Y.Y.K.....QL.R.NRF..L..S.....F.L.V.V.
1F	71	..LL.....F.P.SL.DQ.....S.....VH.N.N.Y.E.H.KS..LQL.E..RH.....S.....P.....F...L.
24A	68	.I.....AAFSNP..L.TS.....R..K..H.S.N.Y.Y.F.K.....QL..YI.N.A.....S.....V.....M..LEY.
167/24	67	.I.I..DE.SNP..S.ESV.....R..K..YK.....Y..F.....QL.....M.TRA..S..S.....E...K..V.....Q.LVEY.
24B	66	.I.....AAFSNP..L.TS.....R..K..H.N.I.Y.Y.Y.K.....QL.....QM.N.A.....SS.....R.....V.....A.NLEL.

Figure 13

Amino Acid Sequence

Sequence Identical
Name Residues

1D9 V _H	117	EVQLVESGGGLVQPKSLKLSAASGFSFNAYAMN--WVRQAPGKGLEWVARIRTKNNNYATYYADSVKDRYTISRDSSEMLFLQNNLKTEDTAMYYCVTF
MRL-RE24BG	86VWWRM.....T.T.....
V(H)22.1	70	..K.E.....G.M.....V.....T.SN.W.S
V11/pBV19B4	66	..K.....G.R.....T.....T.TD.Y.S
Vh7183(Vh69.1)	66	..K.....K.G.....T.SS.T.S
VH10-19	65	D.K.....K.G.....T.SS.T.S
VHE4-psi	65	L.....G.R.....T.SS.S
V(H)50.1	65	..K.....G.....T.....T.SD.Y.Y
V3	65	..K.....GA.R.....S.....T.TD.Y.
V1/pBV132	64	..K.....G.R.....T.....T.SDFY.E
VH283	64	..M.....K.G.....T.SS.T.S
V(H)37.1	63	..K.....K.G.....T.....T.SS.G.S
V13	61	..K.M.....GA.R.....E.....T.TD.Y./S
V-H 441/V441	59	..K.L.....G.....D.SR.W.S
68-5N	59	-----G.....T.SS.G.S
76-1BG/VH7183.9	58	-----K.G.....T.SS.S
61-1P	58	-----G.R.....T.SSFG.H
57-1M/VH7183.12	58	-----K.G.....T.SS.S
V(H)55	56	..K.L.....G.N.....D.SR.W.S
VH7183.13	55	-----K.G.....T.SS.T.S
	S.SS.....F.....Q..Y.....I-
		..S.E.....Q.L.SD...H.E...G.F.....K.SVY.....RA..GI...TG-
		...P...A...LGF..N.A.G.T.E.SA...G.F...N.Q.I.Y...T.RA..S.T...AR-
		...S.E.R...T.SS--GGSY...P...G.F...NAKNT.Y...SS..S...TR-
		...T.E.R...T.SS--GGSY...P...G.F...NAKNT.Y...SS..S...TR-
		...T.E.R...A.S--DGSFI.XP.T.G.F...NAKNT...SS.RY...LR-
		...T.E.R...Y.SN--GGGS...P.T.G.F...NAKNT.Y...SR..S...AR-
		..HRP...P.L.L.N.A.G.I.E.SA.M.G.F...N.Q.I.Y...T.S..S.T...ARD
		...P...R...I.AS.N.A.D.T.E.SA...G.FIV...T.Q.I.Y...A.RA...I...AR-
		...T.E.R...T.SS--GGGN...P...G.F...NAKNN.Y...SS.RS...L...AR-
		...T.E.R...T.SG--GGSY...P...G.F...NAKNN.Y...SS.RS...L...AR-
		...L.R.SP...L.L.N.A.G.T.E.SA...G.F...N.QNI.Y...T.RA.AS.T...AKD
	IGE.NP--DSSTIN.TP.L..KFI...NAKNT.Y...SKVRS...L...AR-
		...T.D.R..L..T.NS--GGG...P...G.F...NAKNT.Y...SS..S...AR-
		...T.E.R...T.SS--GGSY...P...G.F...NAKNT.Y...SS.RS...AR-
		...E.....Y.SS--GSSTI...T.G.F...NPKNT...TS.RS...AR-
		...T.E.R...S.S--GGGS...P...G.F...NARNI.Y...SS.RS...AR-
		..A.....Q..IGE.NP--GSSTIN.TP.L..KFI...NAKNT.Y...SKVRS...L...AR-
		...T.E.R...Y.SN--GGGS...P.T.G.F...NAKNT.Y...SS..S...AR-

Figure 14

[illegible]

Name	ID	Surface	Core	Kabat CDR	FR	FR Surface	Core FR	FR Near CDR	V _K	J Chain	Closest Human Germ-line Gene	L1 Len	L2 Len	L3 Len	L1 Class	L2 Class	L3 Class
1D9 V _K	100.0	30	82	32	82	22	60	33	14	100	14	16	7	9	4	1	1
036521	90.4	27	76	28	75	19	56	31	13	90	13	DPK19-A1+	Same	Same	Same	Same	Same
II.66	78.8	25	67	22	69	18	52	30	13	80	12	DPK18-A17+	Same	Same	Same	Same	?
RPMI6410	78.8	25	67	22	69	18	52	30	13	79	12	DPK18-A17+	Same	Same	Same	Same	?
ZM1-1	78.8	25	66	21	68	18	52	30	13	79	12	DPK18-A17+	Same	Same	Same	Same	Same
VL clone 54	78.1	25	66	21	68	18	52	30	13	79	12	DPK18-A17+	Same	Same	?	Same	Same
HF-21/28	79.3	24	66	21	68	18	52	30	13	78	12	DPK18-A17+	Same	Same	Same	Same	Same
SpA2-08	77.9	24	65	21	68	18	51	30	13	77	12	DPK18-A17+	Same	Same	?	Same	Same
II.30	77.9	24	65	21	68	18	51	30	12	77	12	DPK18-A17+	Same	Same	Same	Same	Same
HUNVK	77.9	24	65	21	68	18	51	30	12	77	12	DPK18-A17+	Same	Same	Same	Same	Same
O-81	75.7	24	65	21	68	18	51	30	12	77	12	DPK18-A17+	Same	Same	10	Same	?
ToP309	74.8	24	64	20	68	18	51	29	12	76	12	DPK12-A2+	Same	Same	10	?	?
ToP218	74.8	24	64	20	68	18	51	29	12	76	12	DPK12-A2+	Same	Same	10	?	?
SpA3-02	76.1	24	63	20	68	18	51	29	12	76	12	DPK18-A17+	Same	Same	?	Same	Same
II.37	75.2	24	63	20	68	18	51	29	12	76	12	DPK18-A17+	Same	Same	Same	Same	Same
CUM	73.9	24	63	20	68	18	50	29	12	75	12	DPK36-Chr22 4	17	Same	Same	3	Same
VL clone 51	74.6	24	62	20	67	18	50	29	12	75	12	DPK18-A17+	Same	Same	Same	?	Same
II.20	75.2	23	62	20	67	18	50	29	12	75	12	DPK18-A17+	Same	Same	?	Same	Same

Figure 16

[illegible]

Figure 17A

Name	ID
John Doe	12345
Jane Smith	67890
Bob Johnson	11111
Alice Brown	22222
Charlie Davis	33333
Eve Wilson	44444
Frank Miller	55555
Grace Taylor	66666
Henry White	77777
Ivy Green	88888
Jack Black	99999
Karen Grey	00000
Leo Gold	10101
Mia Silver	20202
Noah Bronze	30303
Olivia Copper	40404
Peter Iron	50505
Quinn Steel	60606
Rachel Lead	70707
Sam Tin	80808
Tina Zinc	90909
Uma Nickel	01010
Victor Platinum	11111
Wendy Palladium	22222
Xavier Silver	33333
Yara Gold	44444
Zoe Copper	55555

[illegible]

Name	ID	All	Surface	Core	Kabat CDR	FR	FR Surface	Core FR	FR Near CDR	Vernier	V _H	J Chain	Closest Human Germline Gene	H1 Size	H2 Size	H3 Size	H1 Class	H2 Class
1D9 V _H	100.0	117	29	84	30	87	21	65	30	16	100	17		5	19	6	1	4
030094	67.7	86	19	67	15	72	17	57	26	12	75	13	DP-29-122+	Same	Same	16	Same	Same
N51P8	68.3	86	18	66	15	72	16	57	25	12	75	13	DP-29-122+	Same	Same	15	?	Same
IW2-91	67.5	85	18	65	15	72	16	56	25	12	75	12	DP-29-122+	Same	Same	15	Same	Same
H2-46	66.7	84	18	65	15	72	16	56	25	12	75	12	DP-29-122+	Same	Same	15	Same	Same
039158	72.2	83	17	64	15	71	15	56	25	12	74	12	DP-29-122+					
038064	65.6	82	17	64	14	71	15	56	25	11	74	12	VH26Rabbits+					
038062	64.6	82	17	63	14	71	15	56	25	11	73	12	VH26Rabbits+					
32.B9	64.6	82	17	63	14	71	15	56	25	11	72	12	VH26Rabbits+	Same		19	Same	3
038062	64.6	82	17	63	14	71	15	56	25	11	72	12	VH26Rabbits+					
034514	69.8	81	17	63	14	70	15	56	25	11	72	12	VH26Rabbits+					
038066	65.3	81	16	63	14	70	15	55	25	11	71	12	VH26Rabbits+					
035365	65.9	81	16	63	14	70	15	55	25	11	71	12	VH26Rabbits+					

Figure 18A

Name	ID	All	Surface	Core	Kabat CDR	FR	FR Surface	Core FR	FR Near CDR	Vernier	V _H	J Chain	Closest Human Germline Gene	H1 Size	H2 Size	H3 Size	H1 Class	H2 Class
Hb-5	69.2	81	16	63	14	69	15	55	25	11	71	12	VH26Rabbits+					
4G12	64.8	81	16	63	14	69	15	55	25	11	71	12	VH26Rabbits+	Same	17	16	Same	3
VH clone 39	66.7	80	16	63	14	69	14	55	25	11	71	12	VH26Rabbits+	Same	17	11	Same	3
040094	62.5	80	16	63	14	69	14	55	25	11	71	12	LSG3.1					
VH clone 18	63.0	80	16	63	13	69	14	55	25	11	71	12	VH26Rabbits+	Same	17	18	Same	3
UB1-24	67.2	80	16	63	13	69	14	55	25	11	71	12	DP-31-V39P+	Same	17	10	Same	3
029764	64.5	80	16	63	13	69	14	55	25	11	71	12	VH26Rabbits+	Same	17	15	Same	3
IW2-105	64.5	80	16	63	13	69	14	55	25	11	71	12	LSG3.1	Same	Same	13	Same	?
UB1-17	65.0	80	16	63	13	69	14	55	25	11	71	11	LSG3.1	Same	Same	12	Same	?
VH clone 41	66.1	80	16	62	13	69	14	55	25	11	71	11	VH26Rabbits+	Same	17	12	Same	3
4B4'CL	67.2	80	16	62	13	68	14	55	25	11	71	11	LSG3.1	Same	Same	8	Same	?
M26	65.0	80	16	62	13	68	14	55	25	11	71	11	LSG3.1	Same	Same	12	Same	?

Figure 18B

Docket No.: 1855.1052-029
 Title: Humanized Anti-CCR2 Antibodies...
 Inventors: Gregory J. LaRosa, *et al.*

Kabat	#	FR or CDR	Mouse 1D9 V _K	Mouse κ-II	Human κ-II	Human Acceptor HF-21/28 (005056)	Surface or Core	1D9 RK _A	1D9 RK _B	Comment
1	1	FR1	D	D*	D		S	D	D	
2	2		V	V	I*		C	V	V	
3	3		V	V	V*		S	V	V	
4	4		M	M	M		C	M	M	
5	5		T	T*	T		C	T	T	
6	6		Q	Q*	Q		C	Q	Q	
7	7		T	T	S	S	S	S	S	
8	8		P	P	P		c	P	P	
9	9		L	L	L		s	L	L	
10	10		T	S	S	S	C	S	S	
11	11		L	L	L*		c	L	L	
12	12		S	P	P	P	c	P	P	
13	13		V	V*	V*		c	V	V	
14	14		T	S	T		c	T	T	
15	15		V	L	P	L	s	L	L	
16	16		G	G	G		c	G	G	
17	17		H	D	E	Q	c	Q	Q	
18	18		P	Q	P		s	P	P	
19	19		A	A	A		c	A	A	
20	20		S	S*	S		c	S	S	
21	21		I	I*	I		c	I	T	
22	22		S	S*	S*		C	S	S	
23	23	FR1	L	C	C		C	C	C	
24	24	CDR1	K	R	R	R	s	K	K	
25	25		S	S*	S*		c	S	S	
26	26		S	S*	S		s	S	S	
27	27		Q	Q	Q		s	Q	Q	
27A	28		S	S	S		s	S	S	
27B	29		L	L	L		c	L	L	
27C	30		L	V	L	V	s	L	L	
27D	31		Q	H	H	H	c	D	D	
27E	32		S	S	S		s	S	S	
27F			-		x			-	-	
28	33		D	N	D		s	D	D	
29	34		G	G*	G		c	G	G	
30	35		K	N	N	N	c	K	K	
31	36		T	T	N		c	T	T	
32	37		L	Y*	Y	Y	c	F	F	
33	38		L	L*	L		c	L	L	
34	39	CDR1	N	E	N		c	N	N	
35	40	FR2	W	W	W		C	W	W	
36	41		L	Y	Y	F	C	F	L	Δ1

Figure 19A

Docket No.: 1855.1052-029
 Title: Humanized Anti-CCR2 Antibodies...
 Inventors: Gregory J. LaRosa, *et al.*

Kabat	#	FR or CDR	Mouse 1D9 V _K	Mouse κ-II		Human κ-II	Human Acceptor HF-21/28 (005056)	Surface or Core		1D9 RK _A	1D9 RK _B	Comment
37	42		L	L		L	Q	c		Q	L	Δ2
38	43		Q	Q*		Q		c		Q	D	
39	44		R	K		K		c		R	R	
40	45		P	P*		P		s		P	P	
41	46		G	G*		G		s		G	G	
42	47		Q	Q		Q		c		Q	Q	
43	48		S	S*		S		c		S	S	
44	49		P	P*		P		C		P	P	
45	50		K	K		Q	R	c		R	R	
46	51		R	L		L		C		R	R	
47	52		L	L*		L		C		L	F	
48	53		I	I*		I		C		I	I	
49	54	FR2	Y	Y		Y		C		Y	Y	
50	55	CDR2	L	K		L		c		L	L	
51	56		V	V		V	K	c		V	V	
52	57		S	S		S		c		S	S	
53	58		K	N		N		c		K	K	
54	59		L	R		R	N	c		L	L	
55	60		D	F		A	R	c		D	D	
56	61	CDR2	S	S*		S		s		S	S	
57	62	FR3	G	G		G		S		G	G	
58	63		V	V		V		C		V	V	
59	64		P	P		P		C		P	P	
60	65		D	D*		D		S		D	D	
61	66		R	R		R		C		R	R	
62	67		F	F*		F		C		F	F	
63	68		T	S		S	S	C		S	S	
64	69		G	G*		G		C		G	G	
65	70		S	S*		S		C		S	S	
66	71		G	G*		G		C		G	G	
67	72		S	S*		S		s		S	S	
68	73		G	G*		G		C		G	G	
69	74		T	T*		T		C		I	T	
70	75		D	D*		D		C		D	D	
71	76		F	F*		F		C		F	F	
72	77		T	T*		T		c		T	T	
73	78		L	L		C		c		L	L	
74	79		K	K		K		c		K	K	
75	80		I	I		T		c		I	I	
76	81		S	S		S		c		S	S	
77	82		R	R*		R		s		R	R	
78	83		V	V		V		c		V	V	
79	84		E	E		E		s		E	E	
80	85		A	A*		A		c		A	A	
81	86		E	E*		E		s		E	E	
82	87		D	D*		D		c		D	D	
83	88		L	L		V	V	c		V	V	
84	89		G	G*		G		c		G	G	
85	90		V	V		V		c		V	V	
86	91		Y	Y*		Y		c		Y	Y	
87	92		Y	Y		Y		C		Y	Y	
88	93	FR3	C	C		C		C		C	C	

Figure 19B

Docket No.: 1855.1052-029
 Title: Humanized Anti-CCR2 Antibodies...
 Inventors: Gregory J. LaRosa, *et al.*

Kabat	#	FR or CDR	Mouse 1D9 V _K	Mouse κ-II		Human κ-II	Human Acceptor HF-21/28 (005056)	Surface or Core		1D9 RK _A	1D9 RK _B	Comment
89	94	CDR3	W	F		M		c		W	W	
90	95		Q	Q*		Q	M	c		Q	Q	
91	96		G	G		A		c		G	G	
92	97		T	T		L		c		T	T	
93	98		H	H		Q		c		H	H	
94	99		F	V		x		s		F	F	
95	100		P	P*		P	W	c		F	P	
95A			-	P		R				-	-	
95B			-	-		-				-	-	
95C			-	-		-				-	-	
95D			-	-		-				-	-	
95E			-	-		-				-	-	
95F			-	-		-				-	-	
96	101		Y	Y		x	-	c		Y	Y	
97	102	CDR3	T	T*		T	F	c		T	T	
98	103	FR4	F	F*		F		C		F	F	
99	104		G	G		G		c		G	G	
100	105		G	G		Q	Q	c		Q	G	
101	100		G	G		G		c		G	G	
102	106		T	T		T		c		T	T	
103	107		K	K*		K	R	s		R	R	
104	108		L	L		V		c		L	E	
105	109		E	E		E		s		E	E	
106	110		I	I		I		s		I	I	
106A			-	-		-				-	-	
107	111	FR4	K	K*		K	-	s		K	K	

Figure 19C

Docket No.: 1855.1052-029
Title: Humanized Anti-CCR2 Antibodies...
Inventors: Gregory J. LaRosa, *et al.*

Kabat	#	FR or CDR	Mouse 1D9 V _H	Mouse IIIc		Human III	Human Acceptor 4B4'CL (000490)	Surface Or Core		1D9 RH _A	1D9 RH _B	Comment
1	1	FR1	L	E*		E		s		E	F	
2	2		V	V		V		C		V	V	
3	3		Q	K*		Q		s		Q	Q	
4	4		L	L*		L*		C		L	L	
5	5		V	E		V		s		V	V	
6	6		L	E		L		c		E	E	
7	7		S	S		S*		c		S	S	
8	8		G	G		G*		c		G	G	
9	9		G	G		G*		c		G	G	
10	10		G	G*		G		c		G	G	
11	11		L	L		L		S		L	L	
12	12		V	V*		V		c		V	V	
13	13		Q	Q		Q	K	s		K	K	
14	14		F	P		P*		c		P	P	
15	15		K	G		G*	G	s		G	G	
16	16		G	G		G		s		G	G	
17	17		S	S		S*		c		S	S	
18	18		L	M*		L*		c		L	L	
19	19		K	K*		R	R	c		R	R	
20	20		L	E		L		c		L	L	
21	21		S	S		S*		c		S	S	
22	22		L	C		C*		C		G	C	
23	23		A	V		A		c		A	A	
24	24		A	A		A		C		A	A	
25	25		S	S		S*		c		S	S	
26	26		G	G		G		c		G	G	
27	27		F	F		F*		C		F	E	
28	28		S	T*		T	T	C		T	S	Δ1
29	29		F	F*		F		C		F	F	
30	30	FR1	N	S		S	S	S		S	N	Δ2
31	31	CDR1	A	N		S	N	c		A	A	
32	32		Y	Y		Y	A	S		Y	Y	
33	33		A	T		A	W	S		A	A	
34	34		M	M		M		c		M	M	
35	35		N	N		S	S	c		N	N	
35a			-	-		-		c		-	-	
35b		CDR1	-	-		-		c		-	-	

Figure 20A

Docket No.: 1855.1052-029
 Title: Humanized Anti-CCR2 Antibodies...
 Inventors: Gregory J. LaRosa, *et al.*

Kabat	#	FR or CDR	Mouse 1D9 V _H	Mouse IIIc	Human III	Human Acceptor 4B4'CL (000490)	Surface Or Core	1D9 RH _A	1D9 RH _B	Comment
36	36	FR2	W	W	W*		C	W	W	
37	37		V	V	V*		C	V	V	
38	38		R	R	R*		C	R	R	
39	39		Q	Q	Q*		c	Q	Q	
40	40		A	S	A		c	A	A	
41	41		P	P	P		s	P	P	
42	42		G	E	G*		s	G	G	
43	43		K	K	K		s	K	K	
44	44		G	G	G		c	G	G	
45	45		L	L	L*		C	L	L	
46	46		E	E*	E		C	E	E	
47	47		W	W	W*		C	W	W	
48	48		V	V*	V*		C	V	V	
49	49	FR2	A	A	S	G	C	<u>G</u>	<u>G</u>	
50	50	CDR2	R	E	V		c	R	R	
51	51		I	I	I		c	I	I	
52	52		R	R	S	K	s	R	R	
52a	53		I	L	G	S	s	T	T	
52b	54		K	K	K*		s	K	K	
52c	55		N	S	T	T	c	N	N	
53	56		N	H	D	D		N	N	
54	57		N	N	G	G		N	N	
55	58		Y	Y	G	G		Y	Y	
56	59		A	A	S	T	s	A	A	
57	60		T	T	T		c	T	T	
58	61		Y	H	Y	D	c	Y	Y	
59	62		Y	Y	Y		c	Y	Y	
60	63		A	A	A		c	A	A	
61	64		D	E	D	A	s	D	D	
62	65		S	S	S	P	s	S	S	
63	66		V	V	V*		c	V	V	
64	67		K	K	K		s	K	K	
65	68	CDR2	R	G	G*	G	s	D	D	
66	69	FR3	R	R	R*		C	R	R	
67	70		Y	F	F*	F	C	F	F	
68	71		T	T	T		C	T	T	
69	72		I	I*	I*		C	I	I	
70	73		S	S	S*		S	S	S	
71	74		R	R	R*		C	R	R	
72	75		D	D	D		c	D	D	
73	76		D	D	N		C	D	D	
74	77		S	S	S		s	S	S	
75	78		E	K	K	K	s	K	K	
76	79		S	S	N	N	s	N	N	
77	80		M	S	T	T	c	T	T	
78	81		L	V	L		C	L	L	
79	82		F	Y	Y	Y	c	<u>Y</u>	<u>Y</u>	
80	83		L	L	L*		c	L	L	

Figure 20B

Docket No.: 1855.1052-029
Title: Humanized Anti-CCR2 Antibodies...
Inventors: Gregory J. LaRosa, *et al.*

Kabat	#	FR or CDR	Mouse 1D9 V _H	Mouse IIIc	Human III	Human Acceptor 4B4'CL (000490)	Surface Or Core	1D9 RH _A	1D9 RH _B	Comment
81	84		Q	Q*	Q		c	Q	Q	
82	85		M	M	M*		C	M	M	
82a	86		N	N	N		s	N	N	
82b	87		N	N	S	S	s	S	S	
82c	88		L	L	L*		c	L	L	
83	89		K	R	R		s	K	K	
84	90		T	A	A		c	T	T	
85	91		E	E	E		s	E	E	
86	92		D	D	D		C	D	D	
87	93		T	T	T		c	T	T	
88	94		A	G	A*		c	A	A	
89	95		M	T	V	V	c	V	V	
90	96		Y	Y	Y*		c	Y	Y	
91	97		Y	Y	Y*		C	Y	Y	
92	98		C	C*	C*		C	G	C	
93	99		V	T	A	T	C	T	T	
94	100	FR3	T	T	R		C	T	T	
95	101	CDR3	F	G	G	D	c	F	F	
96	102		Y	F	R	S	c	Y	Y	
97	103		G	-	x	L	s	G	G	
98	104		N	-	G	P	c	N	N	
99			-	-	x	P	c	-	-	
100			-	-	S	H	c	-	-	
100 a			-	-	L		C	-	-	
100 d			-	-	S		C	-	-	
100 c			-	-	G			-	-	
100 d			-	-	x			-	-	
100 e			-	-	Y			-	-	
100 f			-	-	Y			-	-	
100 g			-	-	Y			-	-	
100 h			-	-	Y			-	-	
100 I			-	-	H			-	-	
100 j			-	-	Y			-	-	
100 k			-	F	F		C	-	-	
101	105		G	A	D	P	C	G	G	
102	106	CDR3	V	Y	Y		C	V	V	
103	107	FR4	W	W	W*		C	W	W	
104	108		G	G	G*		C	G	G	
105	109		T	Q	Q	Q	S	Q	Q	
106	110		G	C	G*		C	G	G	
107	111		T	T	T*		C	T	T	
108	112		T	L	L	L	C	L	L	
109	113		V	V	V*		C	V	V	
110	114		T	T	T*		C	T	T	
111	115		V	V*	V*			V	V	
112	116		S	S	S*			S	S	
113	117	FR4	S	S	S*			S	S	

Figure 20C

```

-ATGGACTTCGGGTAAACTTGGTTTCTTTGTTGTTTTTATCAAGGIGGCATTTGTGAGGTGCAGCTTGTGAGTCTGGAGGAGGATTGGTGCAGCCTA
TACCTGAAGCCCAATTGAACCAAAAGAAACAACAACAAAAAATAGTTCACACGTAACACTCCACGTCGAAACAATCAGACCCTCCTTAACCACGTCGGAT
100
M D F G L N L V F F V F Y Q G V H C E V Q L V E S G G L V O P
leader ← variable
AAGGTCATTTGAAACCTCAGTGCAGCCCTCTGGATTTCAGCTTCAATGCCATGCACTGGGTCCGCCAGGCTCCAGGAAGGGTTTGGAAATGGGT
200
TTCCAGTAACCTTTGAGAGTACACGTCGGAGACCTAAGTCGAAGTTACGGATGCGGTACTTGACCCAGGCGGTCCGAGGTCCTTTCCCAAACTTACCCA
K G S L K L S C A A S G F S F N A Y A M N W V R O A P G K G L E W V
TGCTGCATAAGAACTAAAAATAATAATTATGCAACATAATTATGCCGATTTCAGTGAAGACAGATACACCAATCTCCAGAGATGATCAGAAAGTATGCTC
300
ACGAGCGTATCTTGATTTTATTATTAATACGTTGTATAATACGGCTAAGTCACCTTTCTGTCTATGTGTAGAGGTCCTCTACTAAGTCTTTTCATACGAG
A R I R T K N N N Y A T Y Y A D S V K D R Y T I S R D D S E S M L
TTTCTGCAAAATGAACAACCTTGAAAACTGAGGACACAGCCAATGATTTACGTGTGACCTTTTACGGTAACGGTGTCTGGGGCACAGGACCCACGGTCACCG
400
AAGACGTTTACTTGTGAACCTTTTGACTCCTGTGTGCGGTACATAATGACACACTGGAAATGCCATTTGCCACAGACCCCCCGTGTCCCTGGTGCCAGTGGC
F L O M N N L K T E D T A M Y Y C V T F Y G N G V W G T T T V T
TCTCTCAGCCAAACAACAGCCCCATCCGTCTATCCCCCTGGT
443
AGAGAGTCGGTTTTTGTGTGCGGTAGGCAGATAGGGGACCA
variable ← constant
V S S A K T T A P S V Y P L V

```

Figure 21

Figure 22

Mfe I |
GAGGTGCAATTGGTTGAGTCTGGAGGAGGATTGGTGAAGCCTGGGGGGTCATTGAGACATCATGTGCAGCCTCTGGATTCACTTTTCAGTGCCTACGCCA
CTCCACGTTAACCAACTCAGACCTCCTCCTAACCACTTCGGACCCCTCCAGTAACCTCTGAGAGTACACGTCGGAGACCTAAGTGAAAGTCACGGATGCGGT
10
E V Q L V E S G G G L V K P G G S L R L S C A A S G F T F S A Y A
TGAAC TGGGTC CGCCAGGCTCCAGGAAGGGTTTGGAA TGGGTGGCCGCAT AAGAACTA AATAA TTAATGCAACATATTA TATGCCGATTCAGTGAA
20
ACTTGACCCAGGCGGTCCGAGGTCTTCCCAACCTTACCCAAACCGGGTATTCCTGATTTTATTATTAATACGTTGTATAATAACGGCTAAGTCACIT
M N W V R Q A P G K G L E W V G R I R T K N N N Y A T Y Y A D S V K
AGACAGATTCACCATCTCCAGAGATGATTCAAAAACACAGCTCTATCTGCAAA TGAACAGCTTGAAAAC TGAAGACACAGCCGCTGTATTACTGTACCACC
30
TCTGCTAAGTGGTAGAGGTCTCTACIAAGTTTTTTGTGCGAGATAGACGTTTACTTGTCGAAC TTTGACTCCIGTIGCGCACATAATGACATGGTGG
D R F T I S R D D S K N T L Y L O M N S L K T E D T A V Y Y C T T
Hsp |
TTTTACGGTAACGGTGTCTGGGGCCAGGGGACCTGGTCACCGTCAGCTCAGCCAAA
357
AAAATGCCATTGCCACAGACCCCGGTCCCTGGGACCAGTGGCAGTCGAGTCGGTTT
F Y G N G V W G Q G T L V T V S S A K

Figure 23

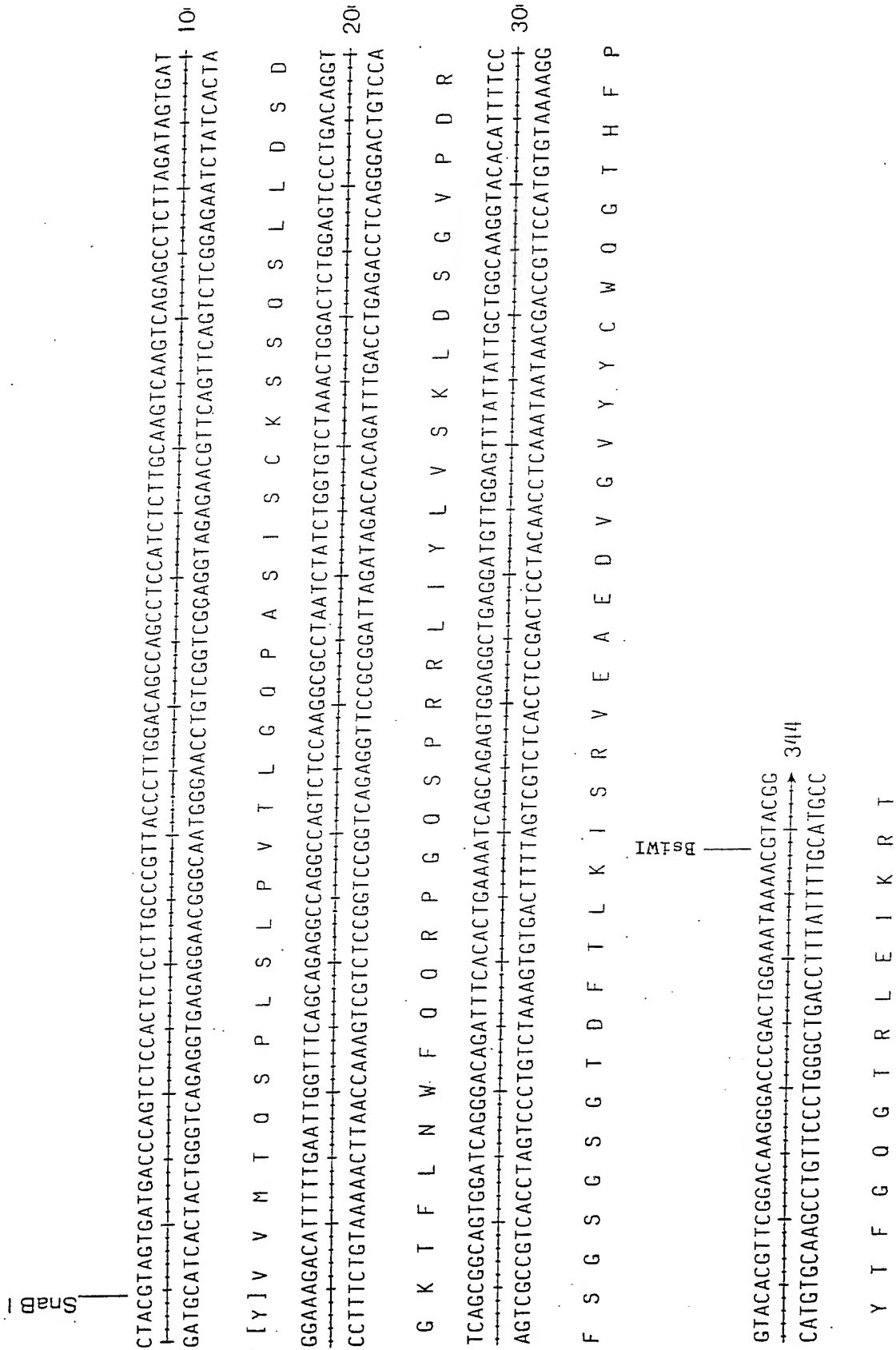
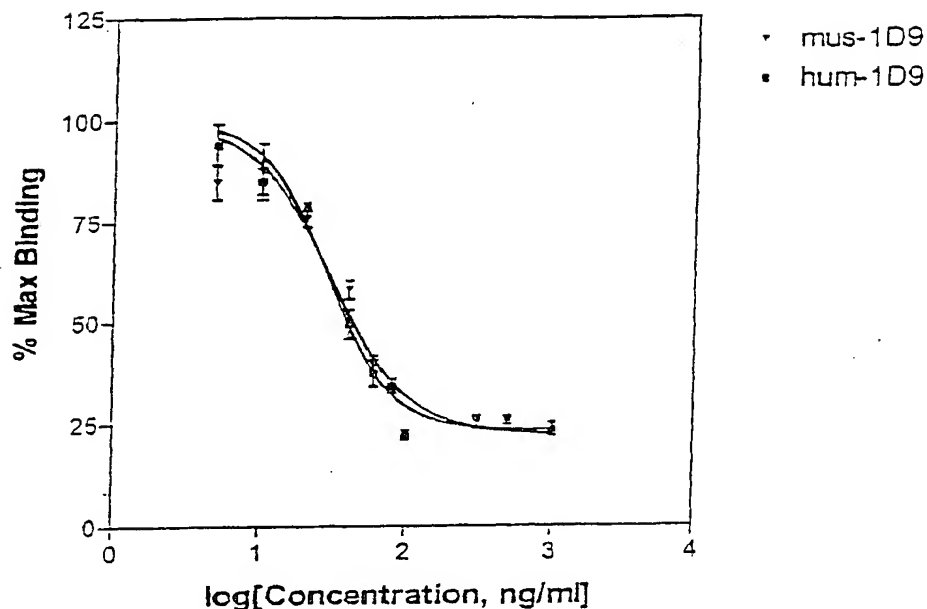


Figure 24

Comparison of Humanized 1D9 vs. m1D9



	hum-1D9	mus-1D9
Equation 1		
Best-fit values		
BOTTOM	23.46	22.40
TOP (Constant)	100.0	100.0
LOGEC50	1.452	1.472
HILLSLOPE	-1.972	-1.627
EC50	28.32	29.68
Std. Error		
BOTTOM	2.656	3.945
LOGEC50	0.04151	0.06251
HILLSLOPE	0.2946	0.3143
95% Confidence Intervals		
BOTTOM	17.18 to 29.74	13.07 to 31.73
LOGEC50	1.354 to 1.550	1.325 to 1.620
HILLSLOPE	-2.668 to -1.275	-2.370 to -0.8835
EC50	22.59 to 35.51	21.12 to 41.71
Goodness of Fit		
Degrees of Freedom	7	7
R squared	0.9931	0.9858
Absolute Sum of Squares	48.60	88.53
Sy.x	2.635	3.556
Data		
Number of X values	10	10
# of Y replicates (mean analyzed)	3	3
Total number of values	10	10
Number of missing values	20	20

Figure 25